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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,883	11/05/2004	Ario DeMarco	3198-101	8674
6449	7590	12/01/2006	EXAMINER	
ROTHWELL, FIGG, ERNST & MANBECK, P.C. 1425 K STREET, N.W. SUITE 800 WASHINGTON, DC 20005			JOIKE, MICHELE K	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 12/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/500,883

Applicant(s)

DEMARCO ET AL.

Examiner

Michele K. Joike, Ph.D.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) 6,12-19,21-40,45 and 46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7-11,20 and 41-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 July 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 5/17/05.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on October 10, 2006 is acknowledged. Claims 1-46 are pending.

Claims 6, 12-19, 21-40 and 45-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 10, 2006.

Claims 1-5, 7-11, 20 and 41-44 are examined.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See paragraph 140.

Claim Objections

Claims 5, 43 and 44 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The test for a proper dependent claim is whether the

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dependent claim includes every limitation of the parent claim. The test is not whether the claims differ in scope. A proper dependent claim shall not conceivably be infringed by anything which would not also infringe the basic claim. See also MPEP § 608.01 (n). Claims 5, 43 and 44 do not include all of the limitations of the parent claim. Claim 1 is a method for the expression of a recombinant protein of interest, said method comprising a) culturing a host cell which expresses ii) at least two genes encoding proteins selected from the group consisting of the chaperone proteins GroEL, GroES, DnaK, DnaJ, GrpE, ClpB and their homologs. Claim 5 has the language a method wherein the genes selected in step a) ii) (of claim 1) include the DnaK, DnaJ, GrpE, ClpB, GroES and GroEL genes or homologs thereof. Claims 43 and 44 have similar language. Since claim 5 depends on claim 1, specifically, step a) ii), at least two genes need to be selected from the group consisting of the chaperone proteins GroEL, GroES, DnaK, DnaJ, GrpE, ClpB. The same rationale applies for claims 43 and 44.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claim 20, the phrase "for example" renders the

claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7, 10, 11, 20 and 41-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Mogk et al.

Applicants claim a method for expressing a recombinant protein by culturing a cell which expresses a gene encoding the recombinant protein and at least two genes encoding chaperone proteins GroEL, GroES, DnaK, DnaJ, GrpE or ClpB, and separating the recombinant protein from the cell culture. Claim 2 limits the Markush group to DnaK, DnaJ and GrpE. In claim 3, one of the genes needs to be ClpB; claim 4 limits the Markush group to GroES and GroEL. Claim 41 limits the Markush group to GroEL, GroES, DnaK, DnaJ, GrpE, claim 42 limits the Markush group to GroEL, GroES, ClpB, and claims 5, 43 and 44 have all 6 genes in the Markush group. The levels of the chaperones need to be controlled and over-expressed from different promoters. The host cell can be *E. coli*.

Mogk et al (EMBO 18(24): 6934-6949, 1999, see entire reference, specifically pp. 6934, 6937, 6942, 6943, 6948 and Table 2) teach in *E. coli*, overexpression of the

following chaperone systems: *dnaK*, *dnaJ*; *groEL*, *groES*; *dnaK*, *dnaJ* and *clpB*.

Plasmids were created to allow for overexpression of the chaperones, as well as tight repression. Various recombinant proteins were expressed (see Table 3) and separated from the cell culture (Materials & Methods).

Claims 1, 2, 4, 5, 7-11, 20 and 41-44 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,159,708.

Applicants claim the method as described above. Claims 8 and 9 further limit the method to wherein levels of the chaperones are controlled from different promoters and using expression systems of different strength.

US 6,159,708, specifically column 3, 5, 6, 9 and Figure 1, teach a plasmid, pG-KJE6, with the *groES,EL* genes in one direction and the *dnaK*, *dnaJ* and *grpE* genes in the other direction. The promoters are *araB* and *Pzt-1*. A T7 promoter, which is a strong promoter, can also be used. Expression of DnaK, DnaJ and GrpE is induced using L-arabinose, and expression of GroEL and GroES is induced using tetracycline. The chaperones can be expressed at different time intervals or at different levels depending on when and how much of the inducers are added. Also, only one set of genes can be induced. The *E. coli* cells are be disrupted, so that the recombinant protein can be isolated and purified.

Allowable Subject Matter


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636


DAVID GUZO
PRIMARY EXAMINER